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Effect of Naringin on myocardial remodeling by regulating the expression of FABP4, FFA in rats with Diabetes cardiomyopathy

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OBJECTIVES To investigate the effect of Naringin on myocardial ultrastructure, serum free fatty acids (FFA) and adipocyte fatty acid binding protein (FABP4) in diabetes cardiomyopathy (DCM) rats, and to explore the possible role of the FABP4 and FFA in the pathogenesis of DCM and cardioprotection of Naringin. To search a novel therapy target for DCM.

METHODS SD rats were randomly divided into normal control group (10 rats), model group (50 rats). Diabetic rats induced by high-sugar and high fat diet and intraperitoneal injection of streptozotocin. Naringin (20/40/80 mg·kg-1·d-1) and atorvastatin (10 mg/kg) were administered in diabetic rats for six weeks. Cardiac weight index were calculated, serum triglycerides, total cholesterol levels were measured by automatic biochemical analyzer, serum FABP4 levels were detected by ELISA kit, serum FFA levels were detected by Copper Color Method. Morphology of myocardial cell and myocardial structure were observed by light microscopy and electron microscopy.

RESULTS Compared with control group, serum triglycerides, total cholesterol level in diabetic rats were significantly higher. After pharmacy intervention for 6 weeks, Naringin and atorvastatin could lower serum triglycerides, total cholesterol levels and cardiac weight index. There were positive correlations between serum FABP4 and FFA ($P < 0.05$). Serum FABP4 and FFA levels in pharmacy intervention groups were reduced significantly versus diabetic groups. Morphology of myocardial cell and myocardial structure were analyzed through light microscopy and electron microscopy, which were improved by naringin treatment.

CONCLUSIONS Naringin could reduce serum glucose, triglycerides and total cholesterol, FABP4 and FFA levels in dose-dependent fashion. In addition, naringin could improve myocardial remodeling and myocardial morphological changes by regulating the expression of FABP4, FFA in rats with diabetes cardiomyopathy. Serum FABP4 might be as an important indicator to predict the severity of 1ipotoxicity in the diabetes, and would be a novel therapy target for diabetic cardiac lipotoxicity.

OBESITY

GW26-e0255

Targeted down-regulation of cardiac CD36 by lentivirus-mediated RNA interference prevents cardiac hypertrophy and systolic dysfunction in high-fat-diet induced obese mice

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OBJECTIVES Fatty acid (FA) catabolism abnormality has been proved to play an important role in obesity-related cardiomyopathy. We hypothesized that cardiospecific suppression of CD36, the predominant membrane FA transporter, would protect against obesity-related cardiomyopathy.

METHODS Four-week-old male C57BL/6J mice received high-fat-diet (HFD) or control-normal-diet for 2 wk and then were subjected to intramyocardial injection with recombinant lentiviral vectors containing short hairpin RNAs to downregulate the expression of either cardiac CD36 or irrelevant gene by RNA interference. After a 10-wk continuation of the diet, biochemical, functional, morphological, histological, and molecular profiles were assessed.

RESULTS HFD administration elicited obesity, cardiac hypertrophy and systolic dysfunction accompanied with elevated serum levels of blood urea nitrogen (BUN), creatinine, fasting serum glucose (FSG), total cholesterol (TC) and triglyceride. Additionally, HFD consumption promoted lipid accumulation and reactive oxygen species (ROS) generation in the cardiomyocytes. Cardiospecific CD36 inhibition protected against HFD induced cardiac remodeling by decreasing heart/body weight ratio, increasing left ventricular (LV) ejection fraction and fractional shortening as well as normalizing LV diameter, without influencing body weight gain. Inhibition of cardiac CD36 also mitigated obesity induced alteration in BUN, creatinine and triglyceride, but had no effect on FSG or TC. Moreover, cardiospecific CD36 deficiency corrected myocardial lipid overaccumulation and intracellular ROS overproduction that were induced by HFD feeding.

CONCLUSIONS Cardiospecific CD36 inhibition protects against the aggravation of cardiac functional and morphological changes associated with HFD induced obesity. CD36 represents a potential therapeutic target for obesity cardiomyopathy.

GW26-e0764

High salt diet elevated the fasting Ghrelin in normal human subject: a novel mechanism of obesity?

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OBJECTIVES Overweight/obesity is a chronic disease that carries an increased risk of hypertension, diabetes mellitus, and premature death. Several epidemiological studies have demonstrated a clear relationship between salt intake and obesity, but the pathophysiologic mechanisms remain unresolved. we hypothesized that salt induced ghrelin elevation contribute to the progression of obesity, which regulate appetite, food intake and fat deposition. We therefore investigated the fasting ghrelin concentration during high salt diet.

METHODS 38 normotensive subjects (aged 25 to 50 years) were selected from a rural community of Northern China. They were sequentially maintained on normal diet for 3 days at baseline, a low-salt diet for 7 days (3 g/day, NaCl), then a high-salt diet for 7 days (18 g/day). The concentration of plasma ghrelin was measured by an immunoenzyme method (ELLSA).

RESULTS High salt intake significantly increased the fasting ghrelin level. It was higher during high salt diet(320.7±30.6pg/ml) than low salt diet(192.5±12.6pg/m). The comparison of ghrelin levels between the different salt diet had significant statistical difference ($P<0.01$).

CONCLUSIONS Our data indicates that high salt diet elevate the fasting Ghrelin in normal human subject, which may be a novel underlying mechanism of obesity.

GW26-e1827

Effect of interaction between PLIN gene polymorphism and open lifestyle intervention on weight-loss in Chinese Han Adults

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OBJECTIVES To exam the effect of interaction between PLIN gene polymorphism and open lifestyle intervention on weight-loss in Chinese Han adults.

METHODS 109 overweight or obese subjects were randomized into the test group (n=56) or control group (n=53), and those who were in the test group received 22-week open lifestyle intervention. Anthropometric and metabolic indexes were measured for all subjects before and after intervention, the genotypes of PLIN1, PLIN4 and PLIN6 were amplified by PCR and sequenced through the first-generation sequencing technologies.

RESULTS All subjects have higher frequency of rare allele C at PLIN1 (0.619), common allele G at PLIN4 (0.606), and common allele A at PLIN6 (0.564), in which PLIN1 and PLIN4, PLIN4 and PLIN6 were in strong linkage disequilibrium (D'>0.9). After intervention, BMI, waist circumference and body fat percent of females were all decreased significantly in test group, and lower than in control group, while only waist circumference of males decreased significantly in the test group ($P<0.05$). Subjects who carried rare allele homozygote of PLIN6 got less weight/fat loss than those with common allele in test group, while those who carried rare allele of PLIN1 increased more weight/fat than those with common allele homozygote in control group($P<0.05$); Females in test group carrying one of rare allele homozygote of PLIN1, PLIN4 and PLIN6 got less weight/fat loss than those with common allele, and carrying the rare allele homozygote haplotype of PLIN1/PLIN4 or PLIN4/PLIN6 got less weight/fat loss than those with other haplotype ($P<0.05$).

CONCLUSIONS The interaction between open lifestyle intervention and PLIN gene polymorphism had direct influence on weight-loss effect in Chinese Han overweight and obese adults.